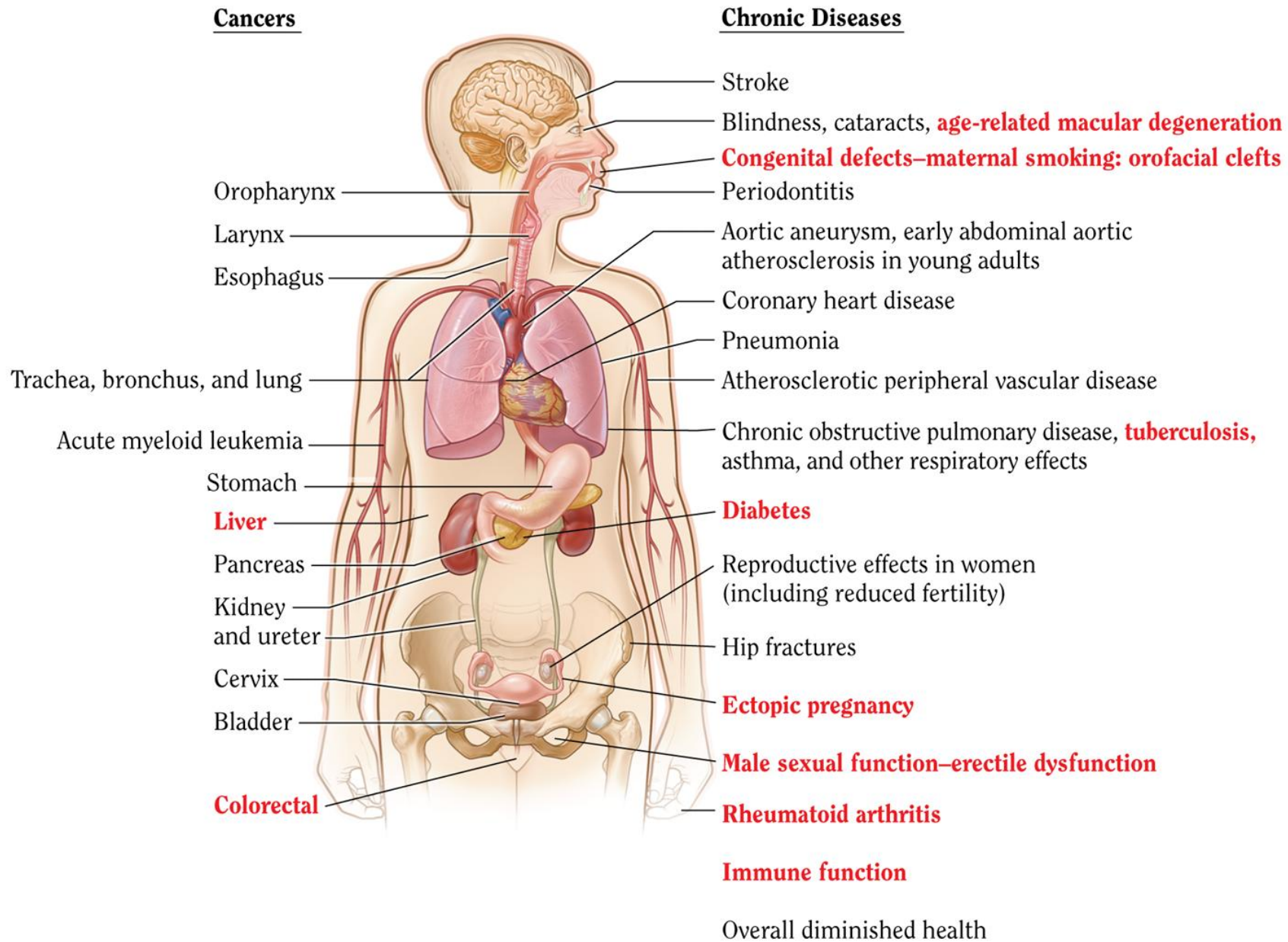


# **Smoking cessation in patients with comorbid diseases**

2025-09-13

분당서울대학교 호흡기내과 강지은

**Figure 1A** The health consequences causally linked to smoking





Contents lists available at [ScienceDirect](#)

## Preventive Medicine

journal homepage: [www.elsevier.com/locate/ypmed](http://www.elsevier.com/locate/ypmed)



### Cigarette smoking and chronic disease in the United States, 2021–2023<sup>☆</sup>

Karin A. Kasza<sup>a,\*</sup>, Richard J. O'Connor<sup>a</sup>, K. Michael Cummings<sup>b</sup>, Martin C. Mahoney<sup>a</sup>

<sup>a</sup> Roswell Park Comprehensive Cancer Center, Elm and Carlton Streets, Buffalo, NY 14263, USA

<sup>b</sup> Medical University of South Carolina, Charleston, SC 29425, USA

Data from the U.S. nationally representative Population Assessment of Tobacco and Health (PATH) Study

- Adults ages 40+years who smoked cigarettes daily in 2021
- Participants with **chronic disease** (n=1261)

Characteristics of the U.S. population of adults ages 40+ who smoke cigarettes daily and have chronic disease, 2021.

Sociodemographic characteristics and cigarette smoking-related characteristics	n	%	95 % CI	
Age group	40–49	281	21.9	19.3, 24.8
	50–59	437	32.8	28.9, 36.9
	60–69	393	30.5	27.4, 33.8
	70+	150	14.8	11.9, 18.2
Sex	Male	469	41.8	38.5, 45.2
	Female	792	58.2	54.8, 61.5
Chronic disease <sup>5</sup>				
Diabetes	688	54.6	51.6, 57.6	
Chronic obstructive pulmonary disease	537	42.8	39.9, 45.7	
Chronic bronchitis	385	29.1	26.0, 32.4	
Cancer	289	24.2	21.5, 27.1	
Emphysema	226	18.7	16.3, 21.3	
Stroke	153	12.5	10.5, 14.7	
Heart attack	151	12.3	10.5, 14.5	
Congestive heart failure	135	10.5	9.0, 12.3	

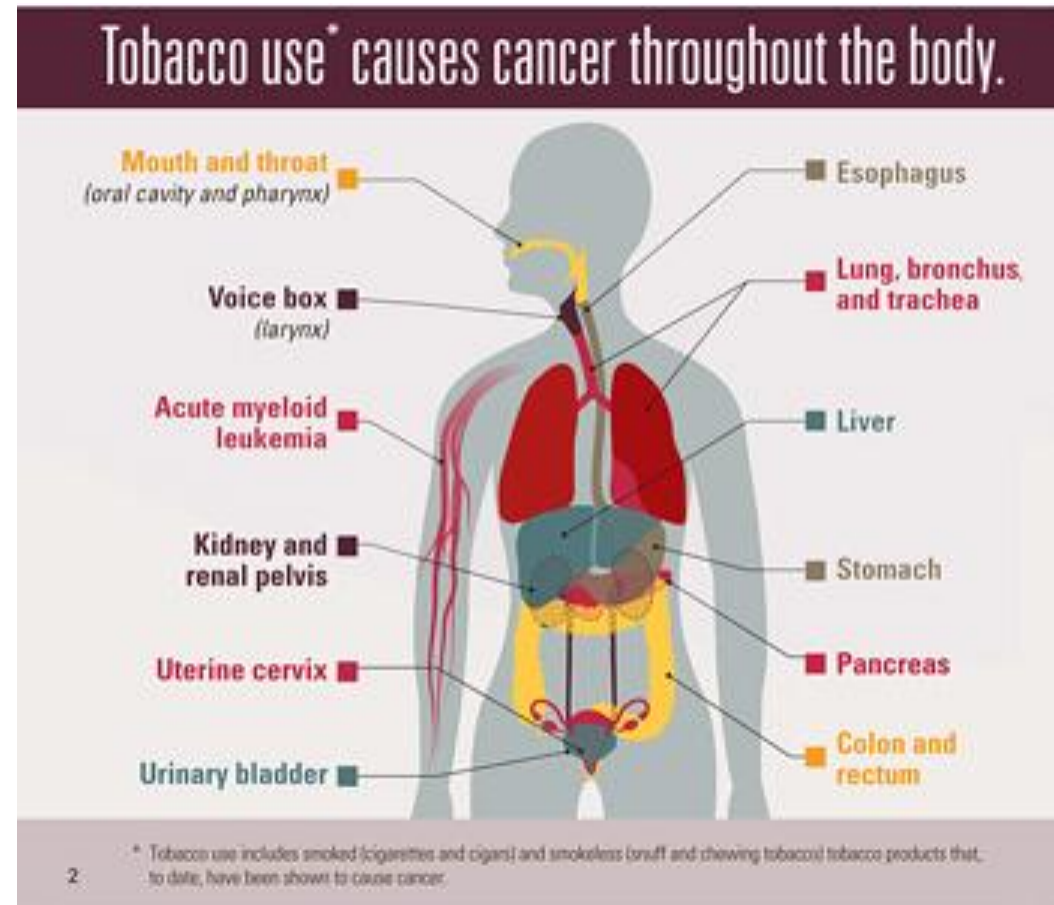
Cigarettes smoked per day	1–9 cigarettes	245	19.9	16.7, 23.5
	10–19 cigarettes	465	35.0	31.3, 38.8
	20+ cigarettes	551	45.2	41.4, 49.0
Also smoke another combustible tobacco product	Yes	137	10.8	9.0, 13.0
Also use a noncombustible tobacco product	Yes	32	2.8	2.1, 3.8
	Yes, within a month	113	8.8	7.3, 10.6
	Yes, between one month and six months	207	15.2	12.6, 18.2
	Yes, between six months and one year	308	23.9	21.3, 26.8
	Yes, more than a year from now	250	20.4	17.8, 23.2
Plan to quit smoking	No, not planning to ever quit	317	26.7	23.8, 29.9
	Don't know/missing	66	4.9	3.8, 6.4
	Yes	762	59.8	57.1, 62.5
Clinician advised to quit in last 12 months?	No	355	27.9	25.4, 30.6
	Other including those who did not see clinician in past 12 months	144	12.3	10.2, 14.7

# Contents

- Cancer
- COPD
- Cardiovascular disease and diabetes

# Cancer

- Well established evidence for **cancer development** associated with cigarette smoking



# Smoking in cancer

- Related to **increased mortality** among cancer patients
  - Current smoking
    - ↑ all-cause mortality by 51%
    - ↑ cancer-specific mortality 61%
  - Former smoking
    - ↑ all-cause mortality 22%
    - No significant effect for cancer-specific mortality

## The Health Consequences of Smoking—50 Years of Progress

A Report of the Surgeon General



U.S. Department of Health and Human Services

# Cancer

- Increased risk for second primary cancers
- Increased risk of recurrence
- Increased risk of poorer response to treatment
- Increased risk of treatment-related toxicity

Smoking promotes tumor progression and increases resistance to chemotherapy



Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

**ScienceDirect**

journal homepage: [www.ejcancer.com](http://www.ejcancer.com)



Original Research

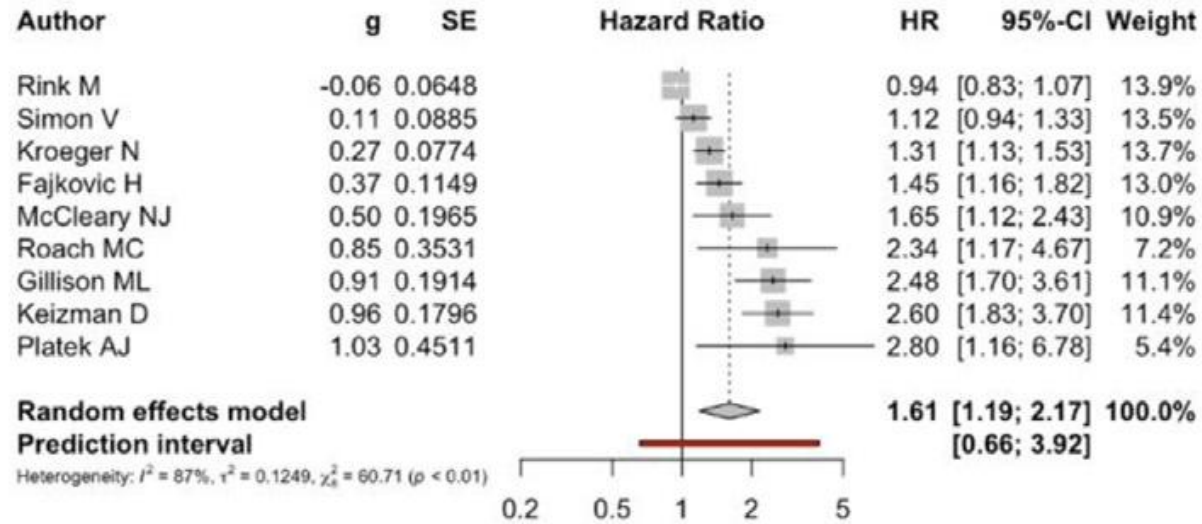
The prognostic impact of the smoking status of cancer patients receiving systemic treatment, radiation therapy, and surgery: A systematic review and meta-analysis



Impact of smoking on mortality in patients undergoing cancer treatment

- 12 reports including data from 31,785 patients with 6 different cancer types
- Lung, head & neck, bladder, breast, kidney and colon cancer

A

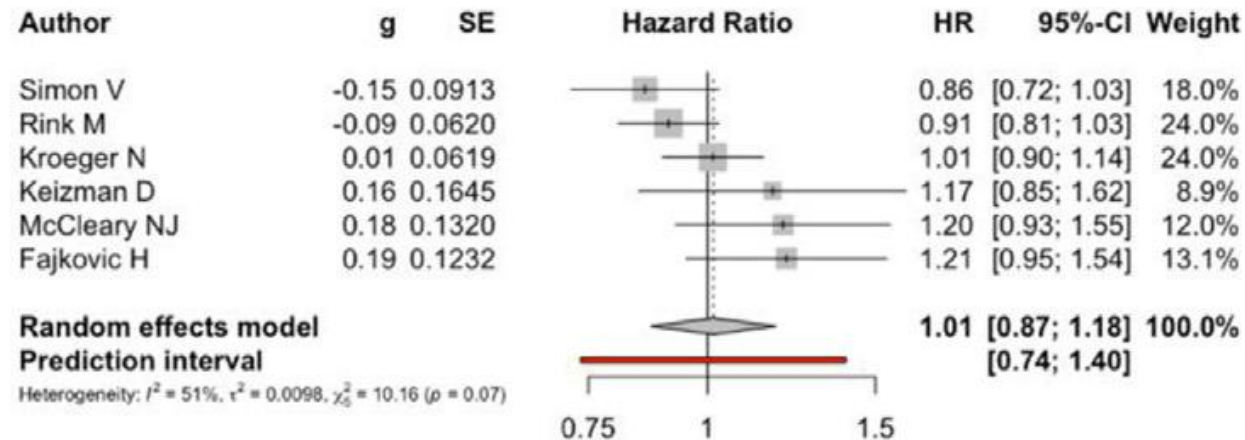


**Active smoking during cancer treatment vs. former or never smokers**

Overall mortality

HR 1.61 (1.19–2.17)  $p=0.007$

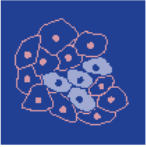
B



**Quit smoking during cancer treatment vs. former or never smokers**

Overall mortality

HR 1.01 (0.87–1.18)  $p=0.818$



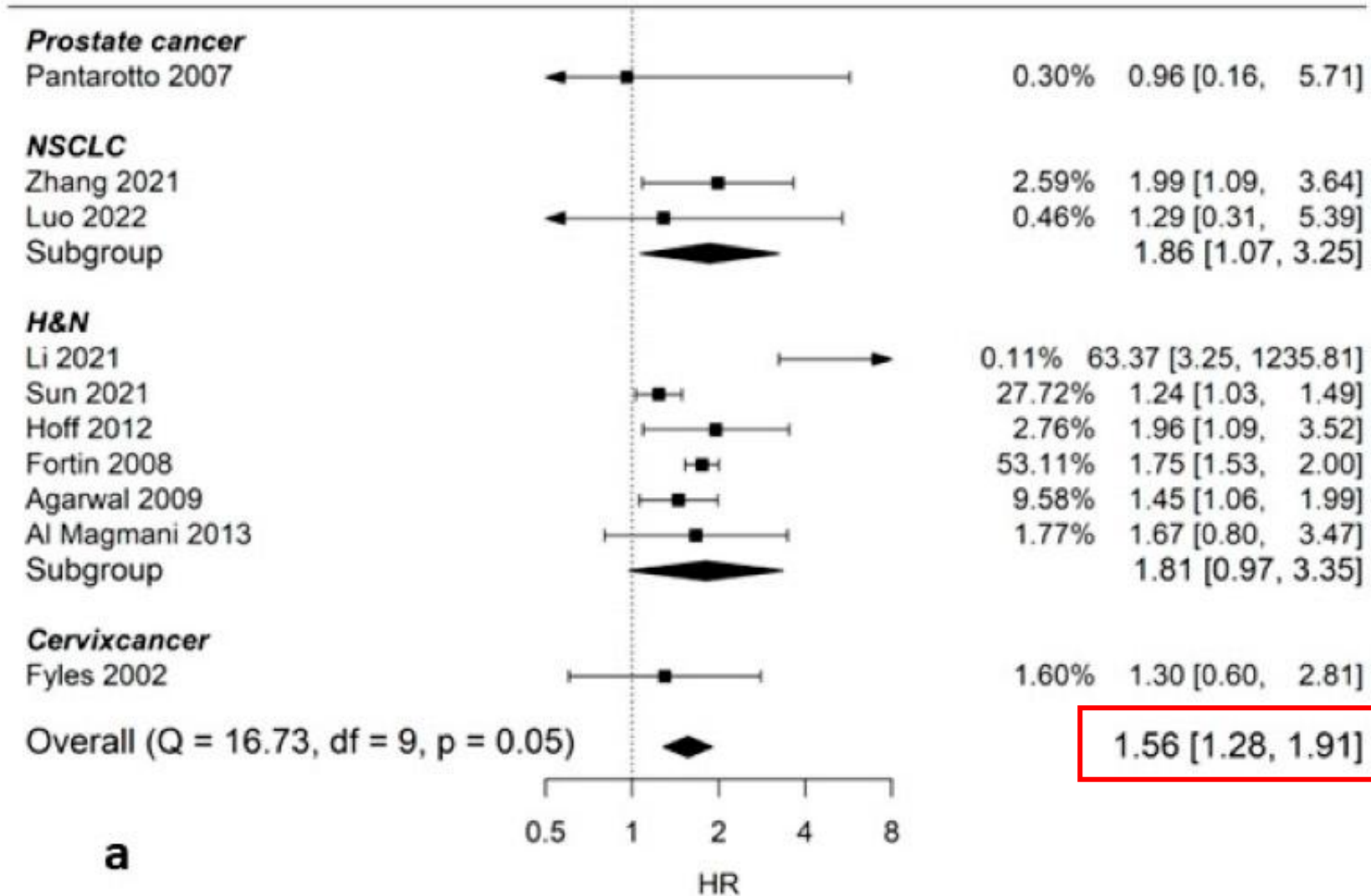
*Systematic Review*

# Effect of Smoking on Treatment Efficacy and Toxicity in Patients with Cancer: A Systematic Review and Meta-Analysis

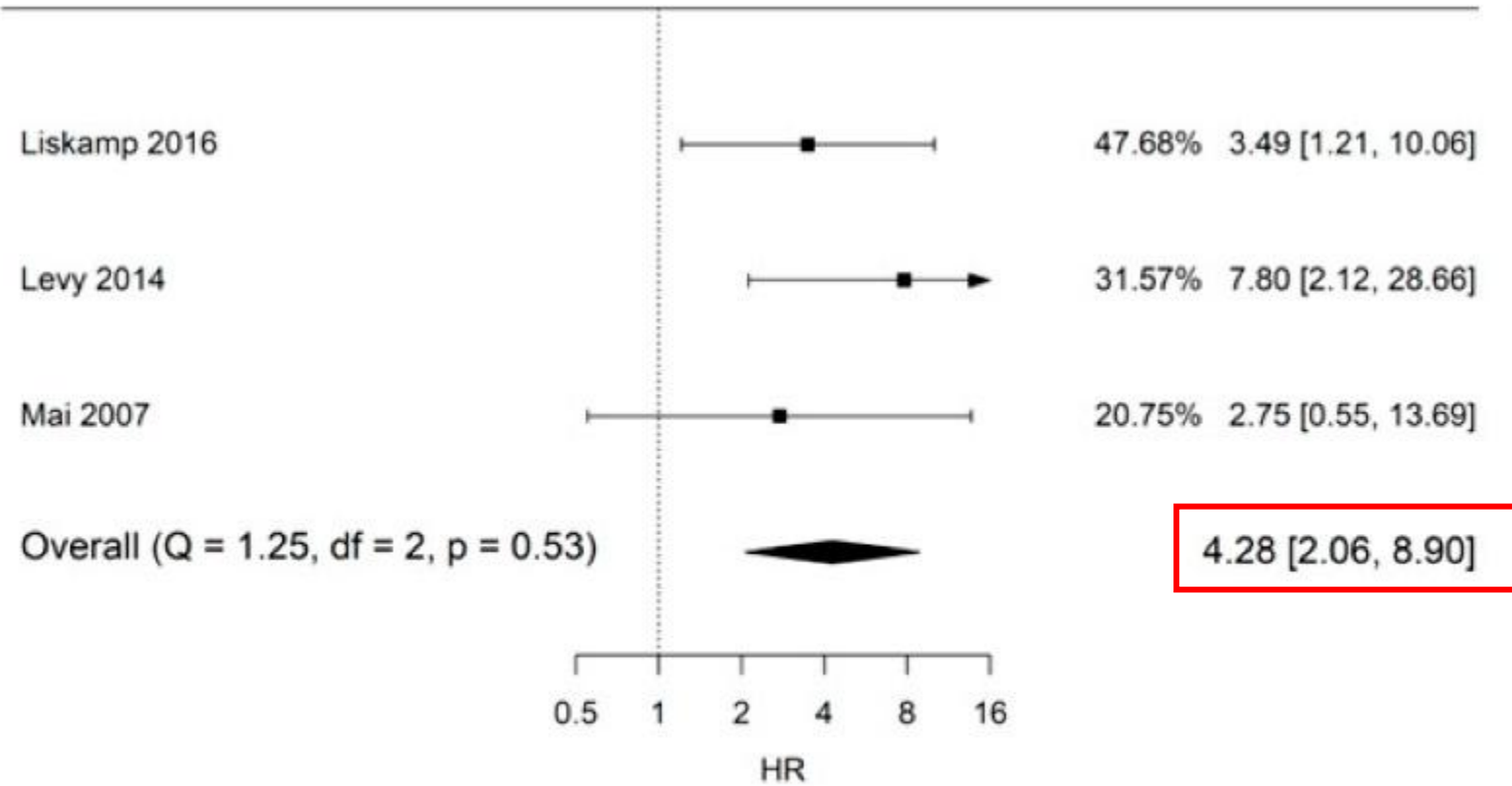
Marie Bergman <sup>1,†</sup>, Georgios Fountoukidis <sup>2,†</sup>, Daniel Smith <sup>3</sup>, Johan Ahlgren <sup>4</sup>, Mats Lambe <sup>4,5</sup>  
and Antonios Valachis <sup>2,\*</sup>

- 79 studies which reported multivariable analysis for the association between smoking and **treatment efficacy or toxicity**

# Smoking during radiotherapy and locoregional recurrence

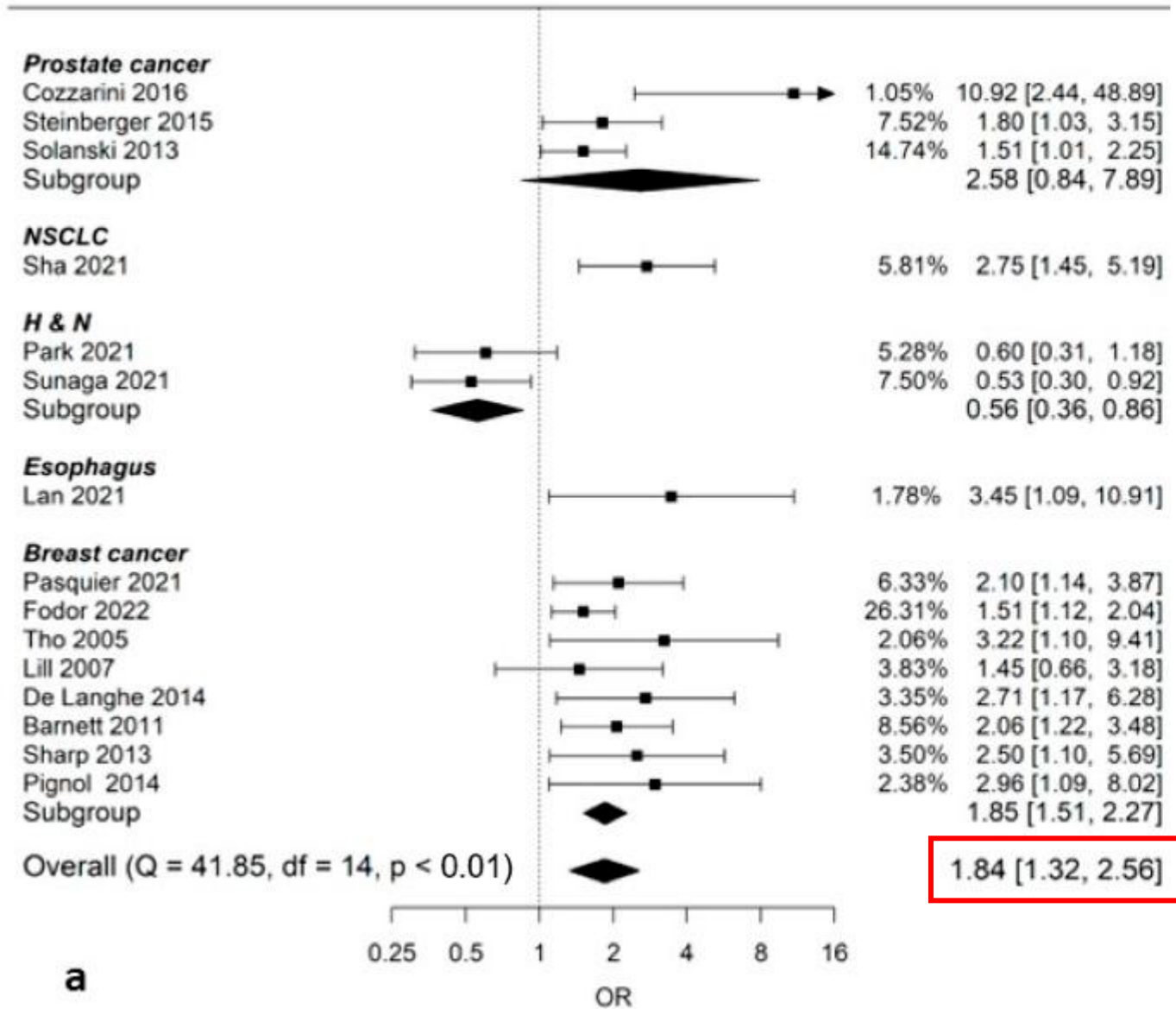


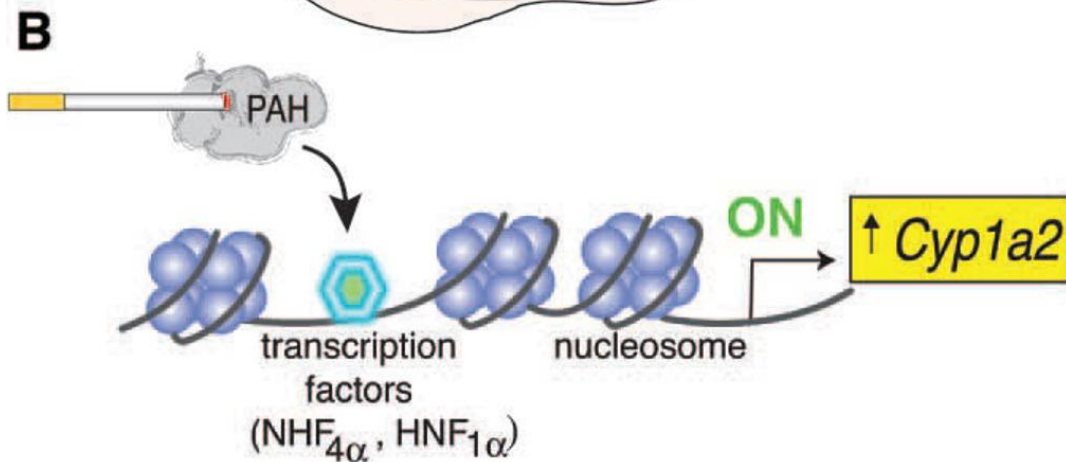
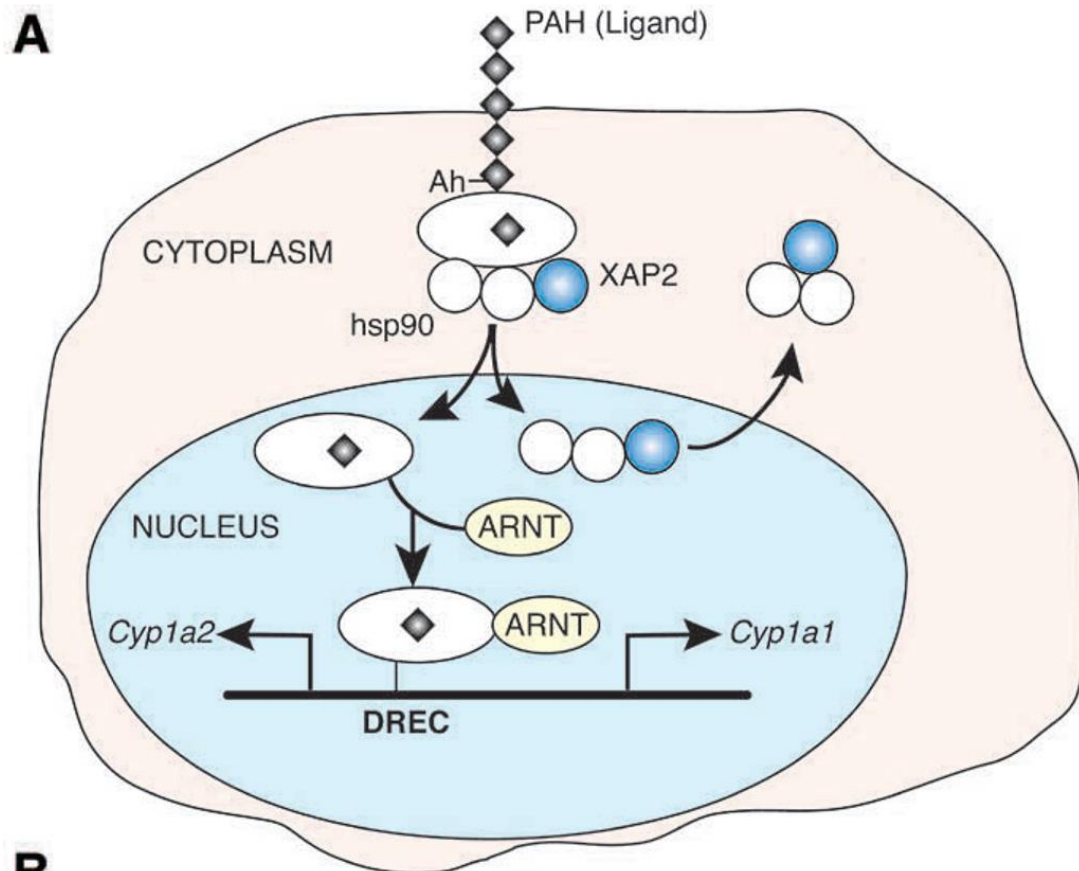
# Smoking during chemoradiotherapy and locoregional recurrence risk



**a**

# Smoking during radiotherapy and treatment-related toxicity





## Smoking induces cytochrome P450 enzymes

→ accelerate the **metabolism** and **clearance** of several chemotherapeutic agents, such as irinotecan and erlotinib

→ potentially leading to **sub-therapeutic** drug levels and **reduced efficacy**

## Chemotherapy with taxanes (docetaxel, paclitaxel) and gemcitabine

→ smokers tend to experience less chemotherapy-induced neutropenia and leukopenia, which may reflect lower drug exposure and could be a surrogate for reduced antitumor effect

# Addressing smoking cessation in cancer patients

- Patients diagnosed with cancer are often **motivated** to change health behaviors to improve their outcomes

Themes identified as **motivators** for and barriers to quitting smoking among survivors of smoking-related cancers

Theme	Sample Quotation
Motivators for Quitting	
<b>Knowing I have cancer</b>	<p>“It has made it a lot easier because I am very motivated. Once you go through chemotherapy and five to six weeks of radiation, and feel like you want to die, the last thing you want to do is have to go through that again. That is a heck of a motivator.” – lung/head/neck cancer, quit after diagnosis</p> <p>“I don't want the cancer to spread. The way I understand it, cigarettes or the nicotine is like throwing fertilizer on a flower garden. It makes it grow.” – other smoking-related cancer, quit after diagnosis</p> <p>“When the doctor tells you you've got cancer...I used to be one of those people that thought 'well you've got to die of something.' I realize, now more than ever, those are just words. That is just somebody trying to be a smart aleck. But when the doctor tells you you've got cancer, your whole world changes.” – lung/head/neck cancer, quit after diagnosis</p>
Doctor's advice	<p>“Once the diagnosis was in and the doctor said that, unless I agreed to quit he wasn't going to treat me, it was an easy decision. I was shocked when he told me that statistically, as many as <math>\frac{3}{4}</math> of the people who quit</p>

## Barriers to Quitting

### Hopelessness

“The thought of going ahead and smoking anyway because you are already probably...it is difficult because I think about my colon and stuff. I can't. It's hard. It's very, very hard. That makes me want [a cigarette] because I don't have nobody to talk to.” – other smoking-related cancer, current smoker

“I have quit so many times. The year or two years before, I don't think I was smoking; but then I started again because I felt really stressed and sort of hopeless when I first found out [I had cancer], and just discouraged. I know it's a bad attitude, but I'm so sick anyway, who cares? I might as well smoke since I enjoyed it for so many years. Out of stress and anxiety I started again. Then after the cancer surgery I quit for over a year.” – other smoking-related cancer, current smoker

### Stress

“When I get nervous, if I have a bad day, or some of those things, it makes me want to smoke. That is the first thing I turn to when I have a bad day or things weren't going my way, I would have a cigarette and smoke.” – other smoking related cancer, quit after diagnosis

### Addiction/cravings

“It's very addicting. Gosh, it's addicting. It makes you crazy. It's crazy, but I have actually looked for cigarette butts before, in the ashtray. I've looked for some in my car, under the car seat, to see if maybe one had fallen out of my purse. It's like you tear up the house. It's like you're an addict. It's just bad.” – lung/head/neck cancer, quit after diagnosis

“I was so badly addicted that the nurse caught me trying to slip down to go out because my daughter would take me out with the IV thing rolling it along to go outside and smoke. One time the nurse wouldn't let me go downstairs, so I had a window in my room. I opened it up and climbed out on the roof and smoked.” – other smoking-related cancer, quit after diagnosis

### Habit/routine

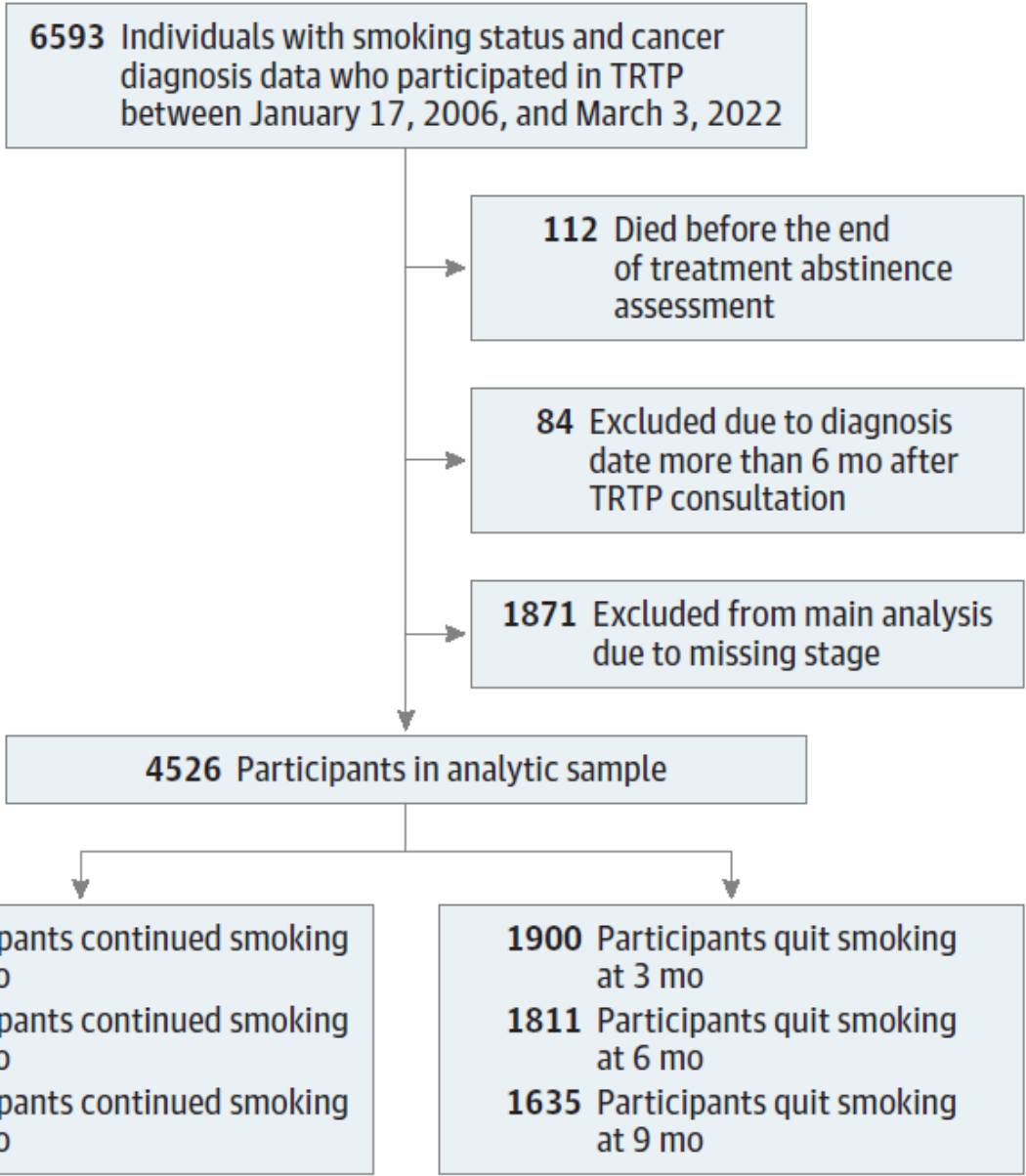
“Smoking is not just one habit. Even though my body had stopped being addicted to the nicotine, I still have to deal with the fact of wanting the cigarette. It is not a physical addiction anymore, but it is very much so a mental addiction.” – lung/head/neck cancer, quit after diagnosis

JAMA Oncology | **Original Investigation**

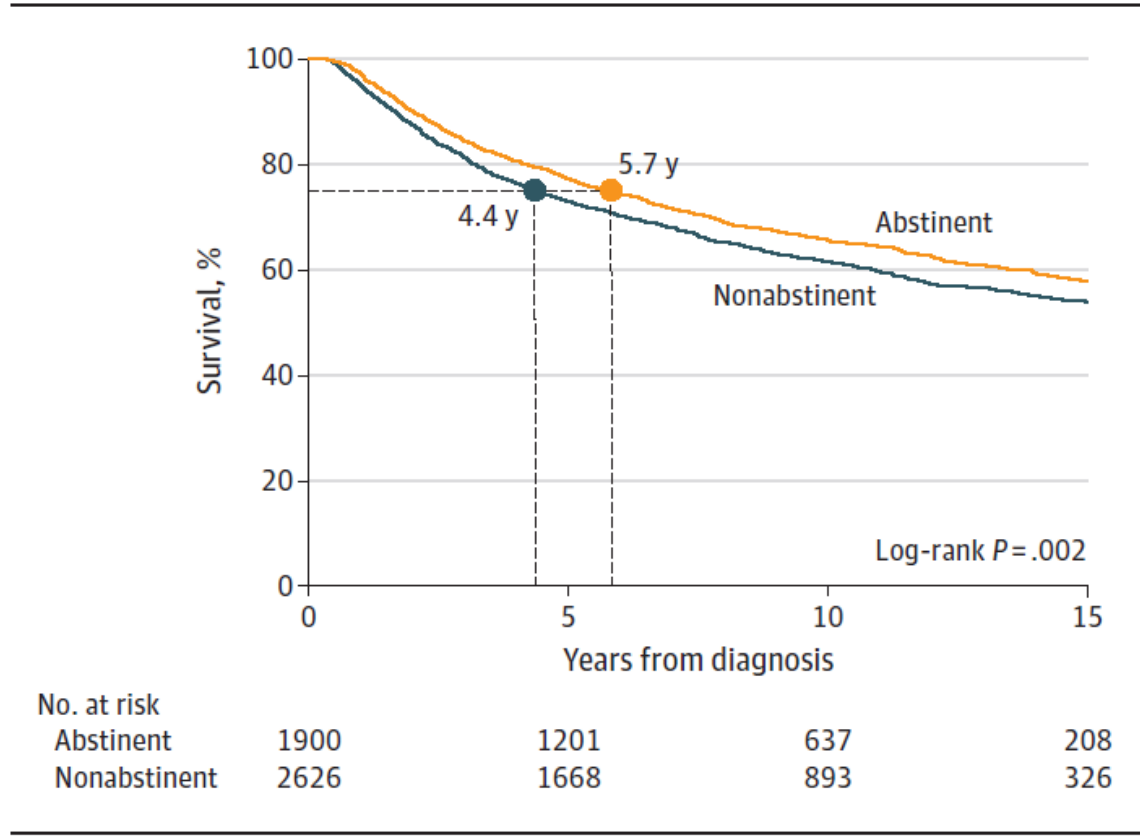
# Survival Outcomes of an Early Intervention Smoking Cessation Treatment After a Cancer Diagnosis

Paul M. Cinciripini, PhD; George Kypriotakis, PhD; Janice A. Blalock, PhD; Maher Karam-Hage, MD;  
Diane M. Beneventi, PhD; Jason D. Robinson, PhD; Jennifer A. Minnix, PhD; Graham W. Warren, MD, PhD

- 4526 currently smoking patients **diagnosed with cancer** and receiving cessation treatment at MD Anderson Cancer Center
- Tobacco Research and Treatment Program (TRTP)
  - Cessation treatment
    - : 6-8 personalized counselling visits and 10-12 weeks of pharmacotherapy (>95% of visits were provided via telemedicine)

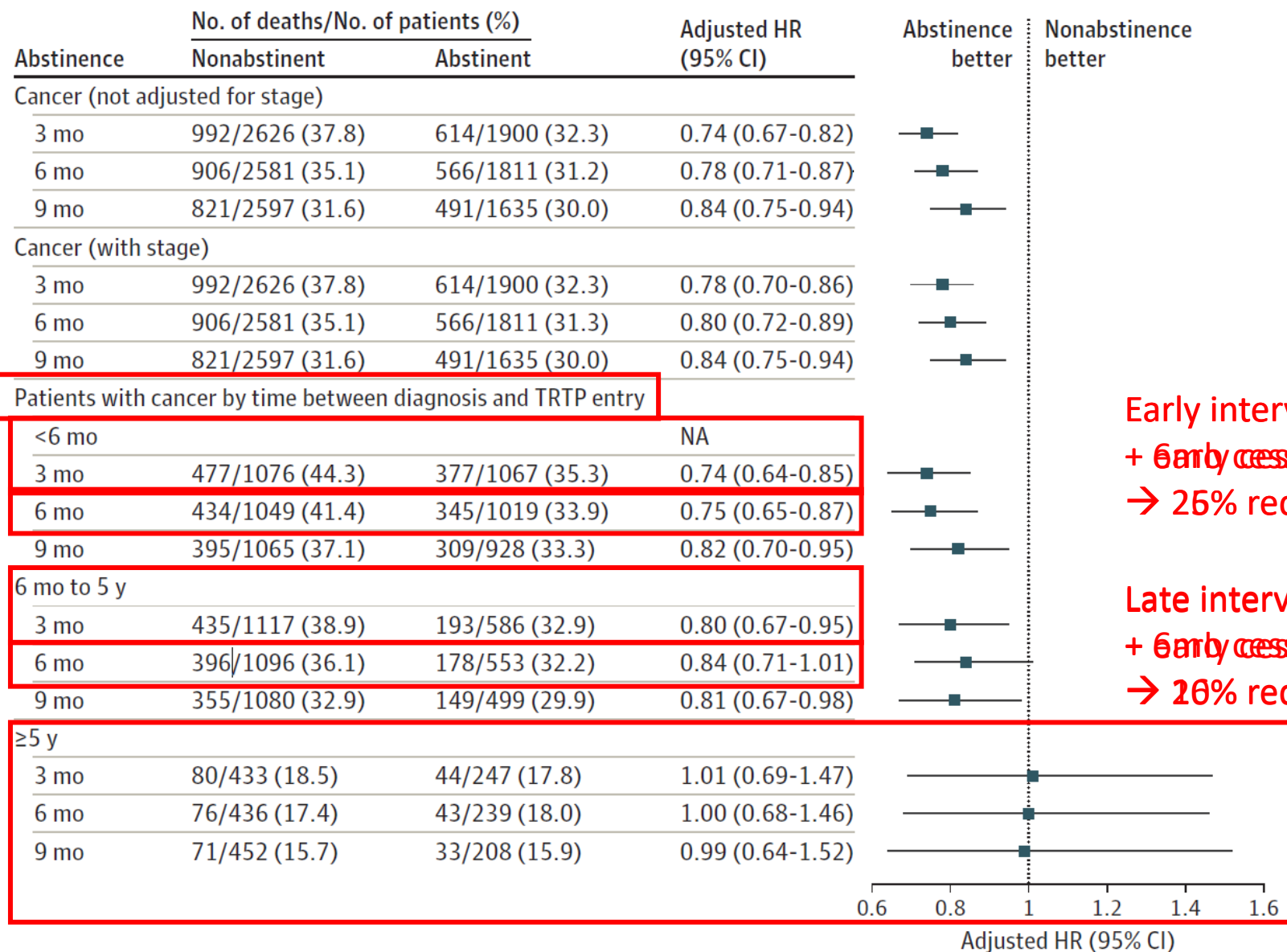


**Figure 2. Overall Survival Outcomes Associated With Smoking Cessation at 3 Months**



The survival outcomes at 3 months were shown without respect to time from diagnosis to entry into the tobacco cessation program among patients with stage information (N = 4526).

Figure 4. Survival Multivariate Analyses According to Cancer Diagnosis and Time Between Diagnosis and Tobacco Cessation Program Entry



Early intervention (<6mo)  
+ 6mo cessation (3mo)  
→ 25% reduction

Late intervention (6mo-5y)  
+ 6mo cessation (3mo)  
→ 26% reduction (not sig.)

# Smoking cessation treatment in cancer patients

- Limited information about
  - which cessation treatments are most effective and cost-effective in patients with cancer
  - how they affect specific cancer outcomes, such as cancer treatment effectiveness, toxicity, and survival
- Cancer patients often take multiple medications that may interact with cessation medications and modification may be needed
  - Major concern: **tamoxifen**
    - **Tamoxifen dose modification is necessary if bupropion is prescribed**
    - Bupropion strongly inhibits CYP2D6 → reduce activation of tamoxifen

# COPD

- Smoking is the single most important risk factor for COPD
  - Development and progression of the disease
- Patients with COPD may be equally motivated to quit smoking but may require more intensive treatment regimens to achieve abstinence compared to people without COPD

# Smoking Characteristics\*

## Differences in Attitudes and Dependence Between Healthy Smokers and Smokers With COPD

Carlos A. Jiménez-Ruiz, MD, PhD; Fernando Masa, MD, PhD;  
Marc Miravittles, MD, PhD; Rafael Gabriel, MD, PhD;  
José Luis Viejo, MD, PhD; Carlos Villasante, MD, PhD;  
Victor Sobradillo, MD, PhD; and the IBERPOC Study Investigators†

4035 individuals aged 40-69 years in Spain

Table 4—Smoking Characteristics\*

Characteristics	Smokers		p Value
	With COPD (n = 153)	Without COPD (n = 870)	
Cigarettes/d	24.2 (14.4)	18.5 (11.7)	< 0.0001
Fagerström test score	4.77 (2.45)	3.15 (2.38)	< 0.0001
Low dependence (0–3)	51 (33.6)	501 (57.7)	
Moderate dependence (4–6)	58 (37.7)	279 (32.1)	
High dependence ( $\geq 7$ )	44 (28.8)	90 (10.2)	
CO in exhaled air, ppm	19.71 (16.29)	15.38 (12.09)	< 0.0001
Smoke inhalation, No. (%)			< 0.0001
Always	113 (73.9)	609 (70)	
Occasionally	24 (15.7)	161 (18.5)	
Never	12 (7.8)	82 (9.4)	
Do not know	4 (2.6)	18 (2.1)	

\*Values given as mean (SD), unless otherwise indicated.

**Table 5—Phase of Smoking Cessation\***

Characteristics	Smokers		p Value
	With COPD (n = 153)	Without COPD (n = 870)	
Precontemplation, %	76 (49.7)	371 (42.6)	NS
Contemplation, %	20 (13.1)	166 (19.1)	NS
Preparation, %	14 (9.2)	60 (7)	NS
Attempts to quit, %			
Never	52 (34.9)	335 (39.4)	
1–3	65 (43.6)	364 (42.8)	
> 3	32 (21.5)	151 (17.8)	
No answer	4	20	

\*Values given as mean (SD). See Table 2 for abbreviation.

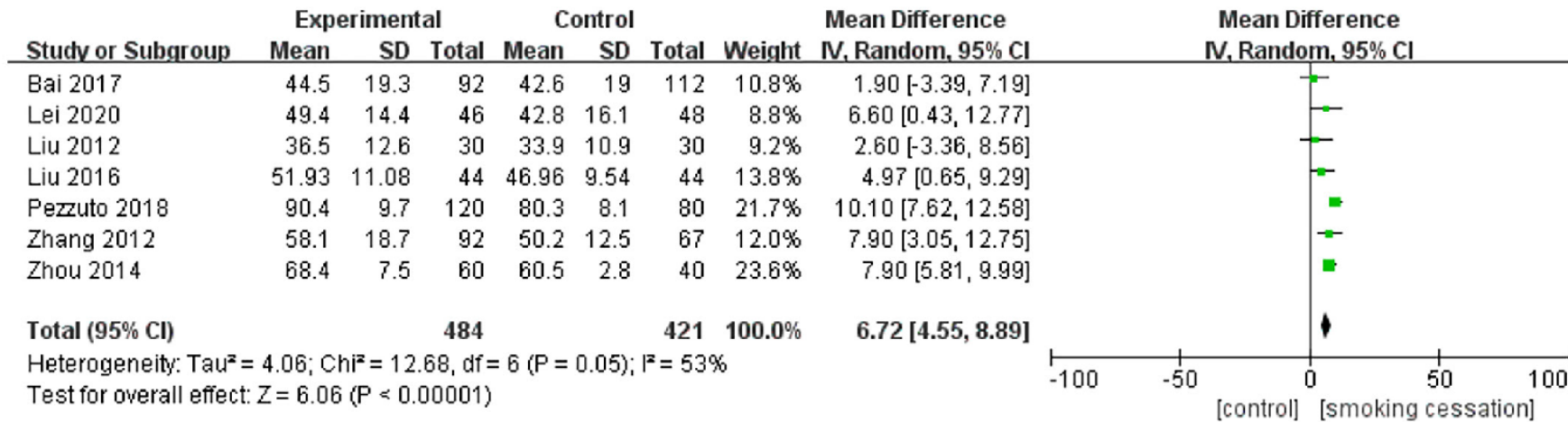
**Table 6—Motives for Stopping Smoking\***

Motives	Smokers		p Value
	Without COPD	With COPD	
Damages health	625 (71.8)	112 (73.2)	NS
Will damage health	490 (56.3)	85 (55.6)	NS
Damages health of others	257 (29.5)	46 (30.1)	NS
Poor example to children	159 (18.3)	22 (14.4)	NS
Unacceptable habit	45 (5.2)	8 (5.2)	NS
Self-affirmation	187 (21.5)	31 (20.3)	NS
Economic	110 (12.6)	13 (8.5)	NS
Others want subject to stop	186 (21.4)	27 (17.6)	NS
Not very hygienic	110 (12.6)	18 (11.8)	NS
No motives	110 (12.8)	15 (9.8)	NS

\*Values given as no. (%). More than one motive could be chosen by each subject. See Table 2 for abbreviation.

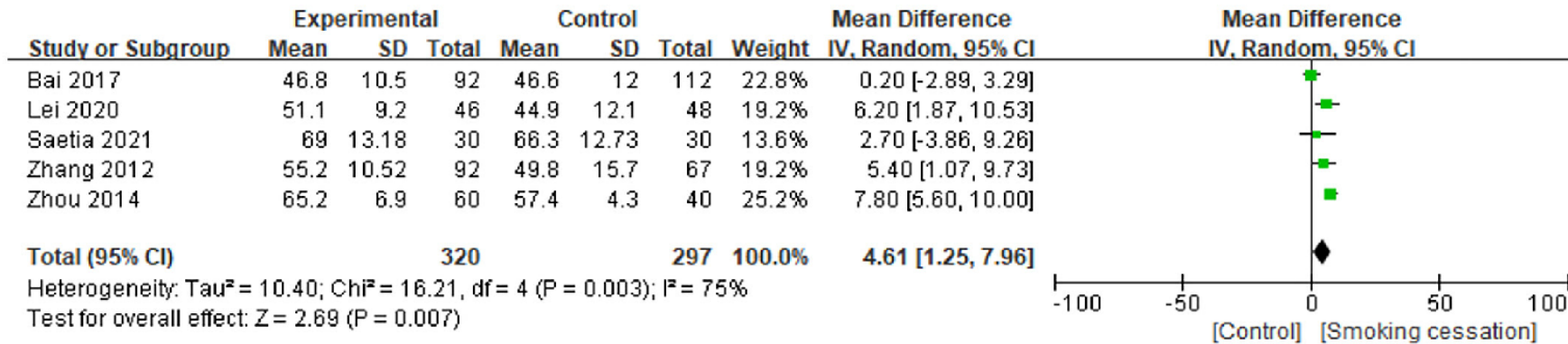
# Effect of smoking cessation in COPD

**A**



Improvement in FEV<sub>1</sub> %  
6.72 (4.55–8.89)

**B**



Increase in FEV<sub>1</sub>/FVC  
4.61 (1.25–7.96)

# Smoking cessation treatment in COPD patients

- Approved cessation treatments are also effective in patients with COPD

# Smoking cessation treatment in COPD patients

**TABLE 6** Meta-analysis of smoking cessation trials in chronic obstructive pulmonary disease patients

Study	Subjects n	Prolonged abstinence rate
<b>Lung Health Study [36]</b>	5887	12 months: 34% <i>versus</i> 9% (NRT)
<b>HILBERINK [37]</b>	392	6 months: 16% <i>versus</i> 9% (NRT)
<b>TØNNESEN [20]</b>	370	12 months: 14% <i>versus</i> 5% (NRT)
<b>TASHKIN [21]</b>	404	6 months: 16% <i>versus</i> 9% (BUP)
<b>WAGENA [38]</b>	255	6 months: 30% <i>versus</i> 19% (BUP)
<b>PEDERSON [39]</b>	64	6 months 27% <i>versus</i> 16%
<b>CROWLEY [40]</b>	49	6 months: 14% <i>versus</i> 14%
<b>BRANDT [41]</b>	56	12 months: 32% <i>versus</i> 16%
<b>TASHKIN [22]</b>	499	12 months: 19% <i>versus</i> 6% (VAR)

Data are presented as abstinence rates for intervention *versus* control groups. NRT: nicotine replacement therapy; BUP: bupropion SR; VAR: varenicline. Reproduced from [35] with permission from the publisher.

**TABLE 7** Efficacy of smoking cessation after 6–12 months from meta-analysis of eight smoking cessation trials in chronic obstructive pulmonary disease patients

Treatment	OR (95% CI)	p-value
<b>Nothing/usual care</b>	1	
<b>Counselling alone</b>	1.82 (0.96–3.34)	0.07
<b>Counselling + antidepressants</b>	3.32 (1.53–7.21)	0.002
<b>Counselling + NRT</b>	5.08 (4.32–5.97)	<0.001
<b>Counselling + varenicline</b>	4.04 (2.13–7.67)	<0.001

Reproduced and modified from [35] with permission from the publisher.

## Smoking cessation for people with chronic obstructive pulmonary disease (Review)

van Eerd EAM, van der Meer RM, van Schayck OCP, Kotz D

Cochrane systematic review - 16 studies involving 13,123 participants

Abstinence 12 months Vs. placebo	Nicotine sublingual tablet	RR 2.6
	Varenicline	RR 3.3
	Bupropion	RR 2.0



## Biomedical risk assessment as an aid for smoking cessation (Review)

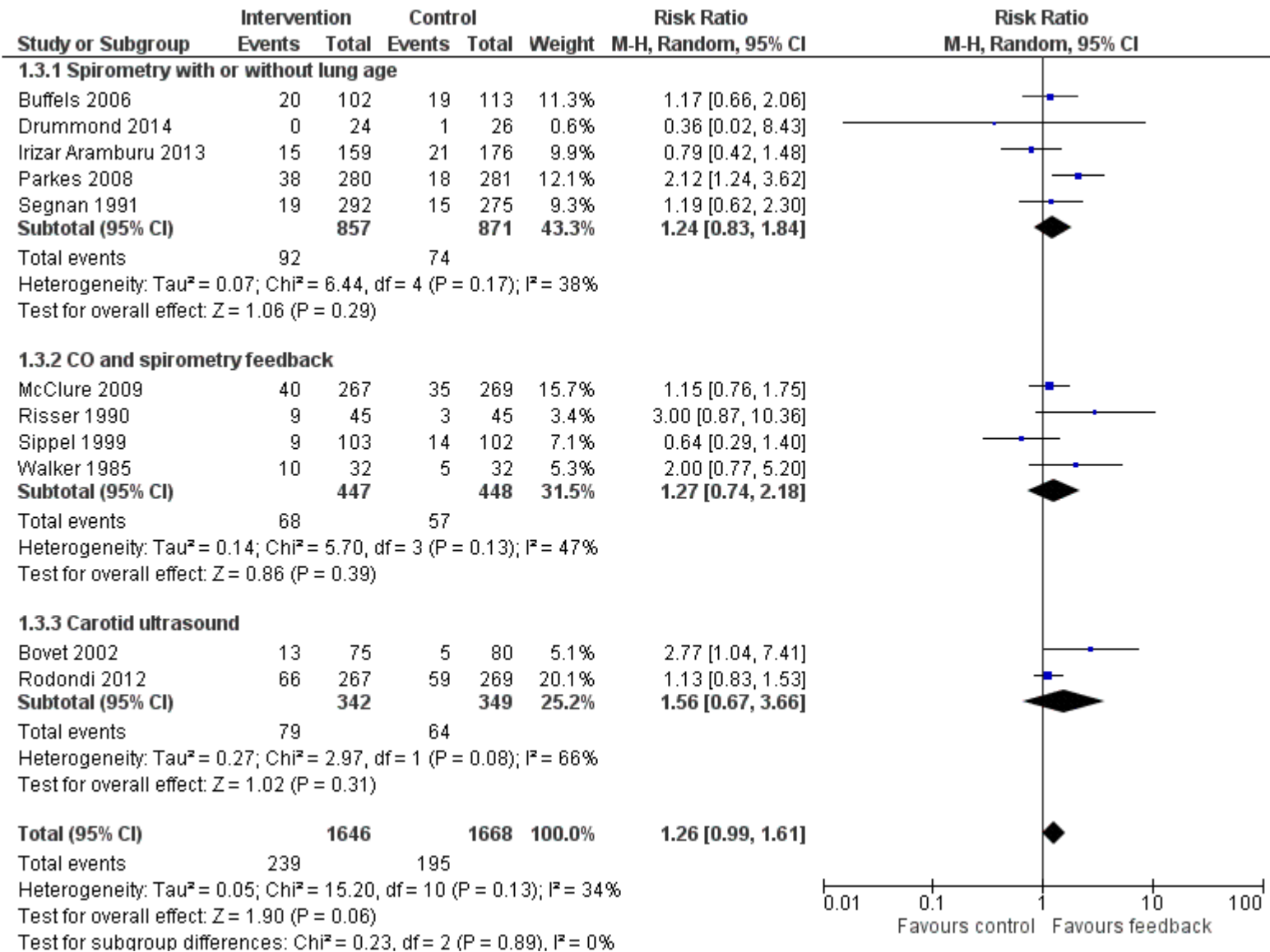
Clair C, Mueller Y, Livingstone-Banks J, Burnand B, Camain JY, Cornuz J, Rège-Walther M, Selby K, Bize R

### Biomedical risk assessment

- Providing smokers with **feedback** on the **current or potential future biomedical effects** of smoking using measurement of exhaled CO, **lung function**, or genetic susceptibility to lung cancer or other diseases

Cochrane systematic review - 20 trials with 9262 participants

# Feedback on smoking-related harm



A sensitivity analysis removing studies at high-risk of bias  
 → significant benefit  
 RR 1.36 (95% CI 1.07-1.74)

# Cardiovascular disease

- Smoking is a serious risk factor for cardiovascular disease and associated mortality
- Rates of cessation using most approved smoking cessation interventions in patients with cardiovascular disease (CVD) are similar to the general population
- NRT, bupropion, and varenicline
  - Have been evaluated in CVD patients and showed effectiveness
  - Several studies evaluated the safety of NRT
  - **Caution** in patients who have **had recent MI (within 2 weeks), and those with serious arrhythmias or unstable angina pectoris**

# Cardiovascular disease

- Smoking cessation should be strongly recommended in patients with CVD
- E-cigarettes
  - Increase the likelihood of successful smoking cessation compared with NRT, but because of lack of long-term safety data and risks of sustained use, e-cigarettes are **not recommended** as first line therapy for smoking cessation
- Complete cessation vs. reduction

# Smoking cessation, but not reduction, reduces cardiovascular disease incidence

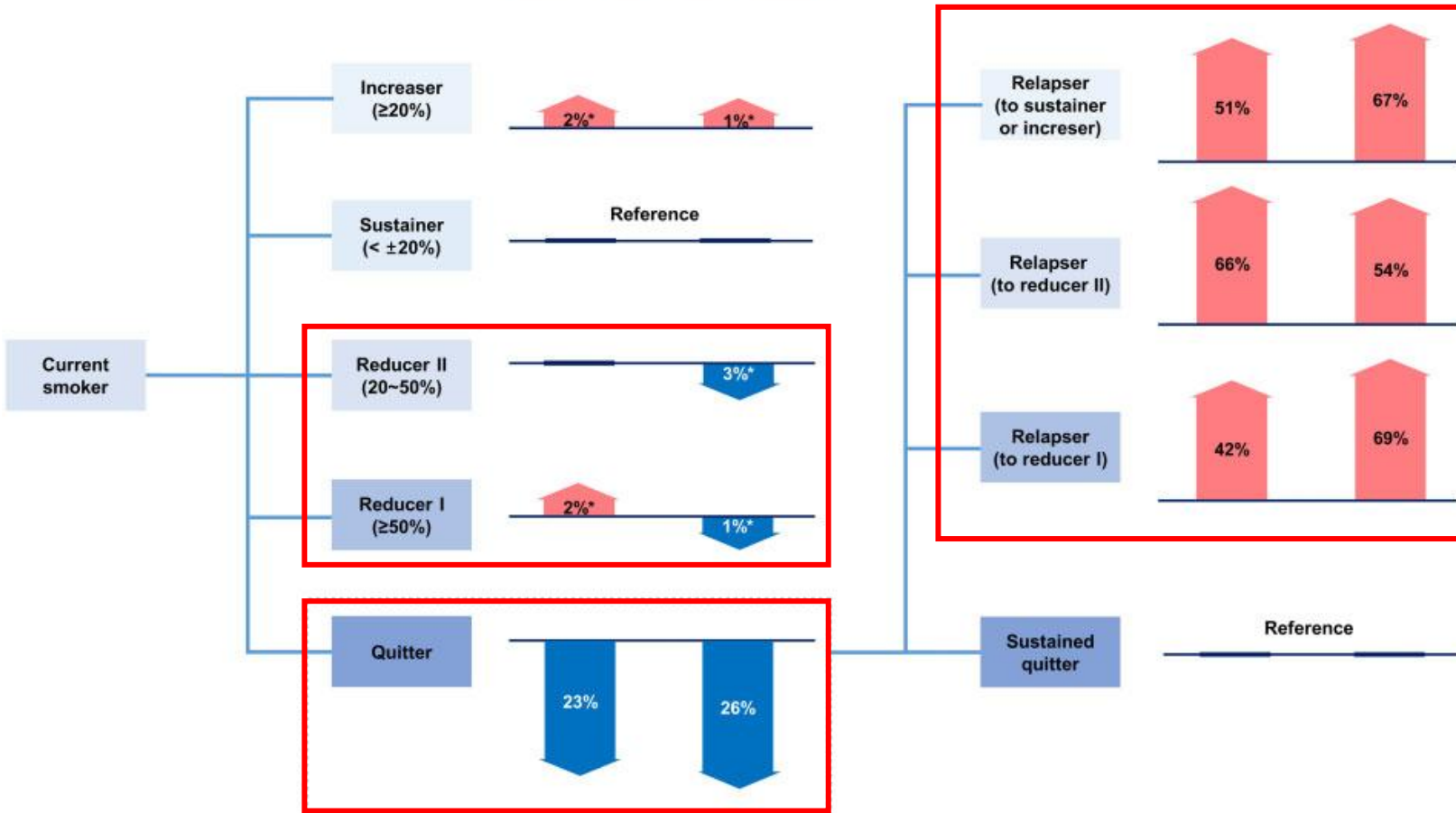
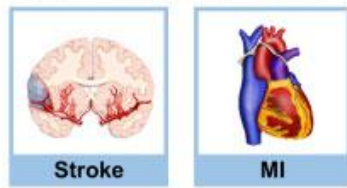
Su-Min Jeong<sup>1†</sup>, Keun Hye Jeon<sup>2†</sup>, Dong Wook Shin <sup>1,3\*</sup>, Kyungdo Han<sup>4</sup>,  
Dahye Kim<sup>5</sup>, Sang Hyun Park<sup>5</sup>, Mi Hee Cho <sup>6</sup>, Cheol Min Lee<sup>7</sup>,  
Ki-Woong Nam<sup>8</sup>, and Seung Pyo Lee <sup>9</sup>

897,975 current smokers aged  $\geq 40$  years who had undergone two consecutive national health examinations (in 2009 and 2011)

- Classified individuals as
  - Quitters (20.6%)
  - Reducers I ( $\geq 50\%$  reduction; 7.3%)
  - Reducers II (20–50% reduction; 11.6%)
  - Sustainers (45.7%)
  - Increasers ( $\geq 20\%$  increase; 14.5%)

Primary analyses  
: Follow-up (mean 6.2 years)

Subgroup analyses  
: Follow-up (mean 4.3 years)



Smoking cessation, but not reduction, was associated with decreased risk of stroke and MI.  
\* No statistical significance

Relapsed smoking was associated with increased risk of stroke and MI compared to sustained quitting.

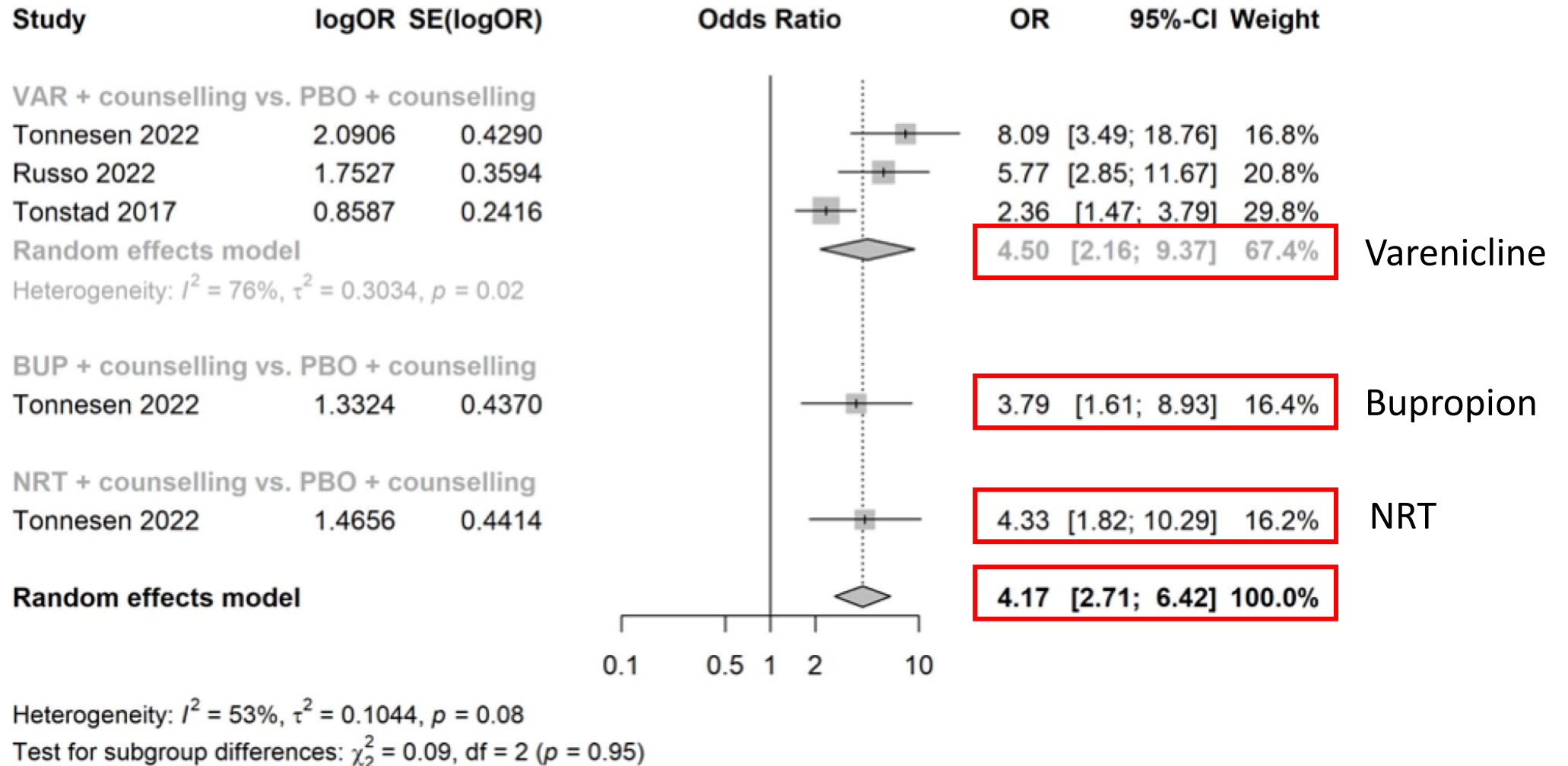
# Diabetes

- Smokers have higher glycosylated hemoglobin (HbA1c) levels than non-smokers
- Smoking as a cause of diabetes
  - Hypothesis: **smoking decreases insulin sensitivity** mediated by nicotine which **stimulates insulin-antagonizing substances** such as cortisol, catecholamines, and growth hormones
- Smoking aggravates the effect of diabetes
  - microvascular and macrovascular complications

# Smoking cessation treatment

- Limited information about specific recommendations regarding the best management approach for diabetic patients
- Not different as the approach in general population

# Smoking cessation treatment in type 2 diabetes



# Post-smoking cessation problems in diabetic patients

- Some studies suggested **diabetes control deteriorates temporarily** during the first year after quitting
- Weight gain after smoking cessation

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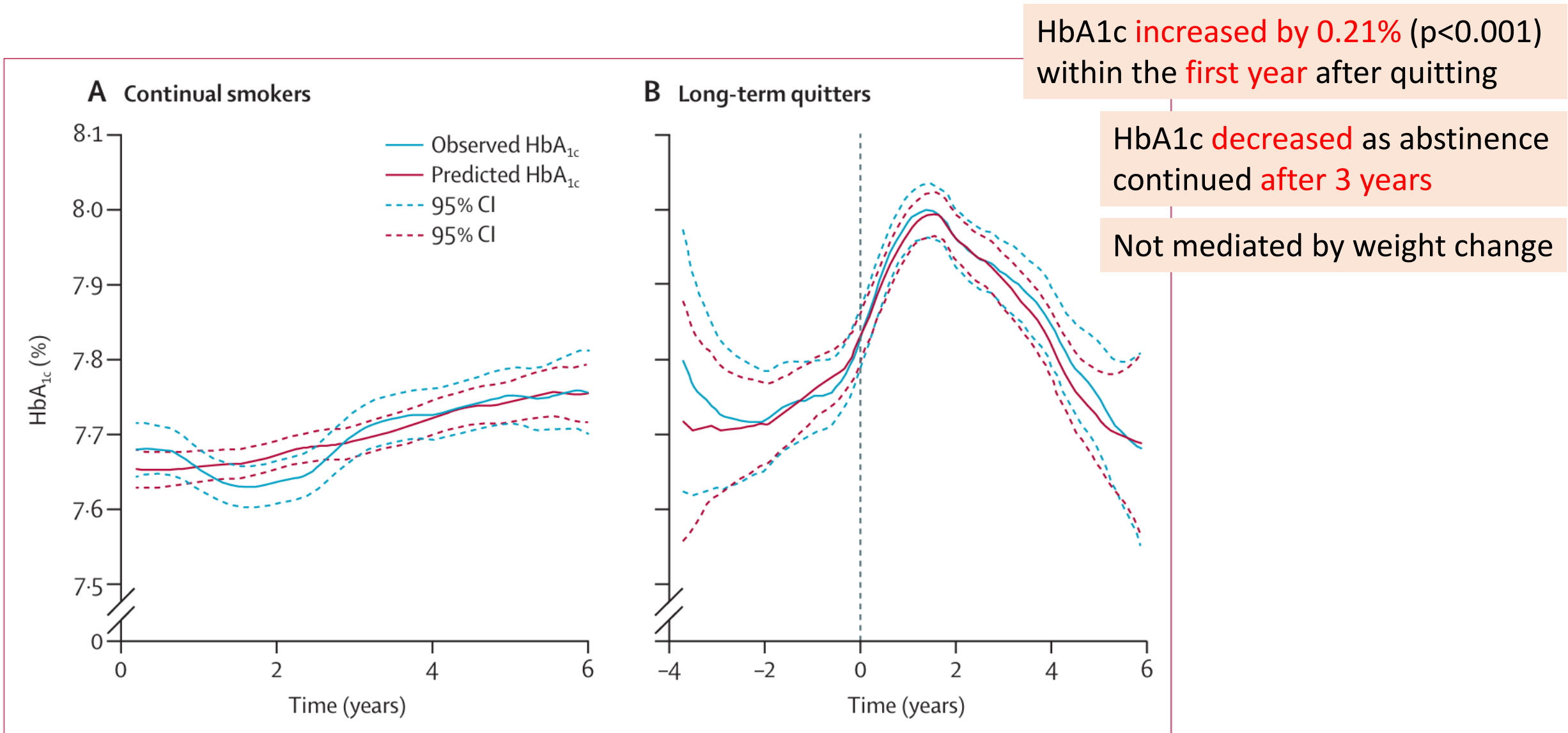
# The association between smoking cessation and glycaemic control in patients with type 2 diabetes: a THIN database cohort study



*Deborah Lycett, Linda Nichols, Ronan Ryan, Amanda Farley, Andrea Roalfe, Mohammed A Mohammed, Lisa Szatkowski, Tim Coleman, Richard Morris, Andrew Farmer, Paul Aveyard*

Retrospective cohort study - adult smokers with type 2 DM in the UK

- 10,692 patients
- 29% quit smoking and remained abstinent for at least 1 year
- Followed HbA1c over time



**Figure 2: Observed and predicted HbA<sub>1c</sub> in continual smokers and long-term quitters**

# Summary

- Smoking is associated with many diseases in the development and progression
- Cancer development and progression, increased mortality, poor treatment response and higher treatment-related toxicity
- Early smoking cessation intervention may be beneficial after cancer diagnosis
- COPD patients may require more intensive treatment due to higher nicotine dependence / biomedical risk feedback?
- Complete cessation rather than reducing smoking to prevent CVD events
- No specific treatment guidelines for patients with chronic diseases
  - Cautions for co-medications, underlying conditions, diabetic control